FORM PTO-1390 REV. 2/01 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

Attorney's Docket Number: 02481.1726
Customer No.: 22,852

U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 09763733

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP99/05980	August 14, 1999	August 29, 1998

TITLE OF INVENTION: MINI-BASKET FOR ANALYZING ACTIVE SUBSTANCE RELEASE FROM A MEDICAMENT FORM

APPLICANT(S) FOR DO/EO/US: 1) Petra LOOS, 2) Brigitte HORLE and 3) Rüdiger MERKEL

Applicants herewith submit to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c)(2)).
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☒ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed with the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371 (c)(2)).
   a. ☒ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154 (d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3)).
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. ☒ Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A Substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821-1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154 (d)(4).
19. ☐ A second copy of the English language translation of the international application 35 U.S.C. 154 (d)(4).
20. ☒ Other items or information:
   a. ☒ Copy of cover page of International Publication No. WO 00/13012
   b. ☒ Request for Approval of Drawing Change and a Copy of New Fig.2

U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 09/763733	INTERNATIONAL APPLICATION NO.: PCT/EP99/05980	ATTORNEY'S DOCKET NUMBER 02481.1726

21. ☒ The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1000.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$860.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search fee (37 CFR 1.445(a)(2)) paid to USPTO **$710.00**

International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$690.00**

International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33 (1)-(4) **$100.00**

	CALCULATIONS PTO USE ONLY	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$860.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).	$	

CLAIMS	NUMBER FILED		NUMBER EXTRA	RATE		
Total Claims	24	- 20 =	4	x $18.00	$72.00	
Independent Claims	3	-3 =	0	x $80.00	$	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				+$270 00	$	
TOTAL OF THE ABOVE CALCULATIONS =					$932.00	
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by ½.					$	
SUBTOTAL =					$932.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest priority date (37 CFR 1.492(f)).					$	
TOTAL NATIONAL FEE =					$932.00	
Fee for recording the enclosed assignment (37 CFR 1.21 (h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property. +					$40.00	
TOTAL FEES ENCLOSED =					$972.00	
					Amount to be refunded:	$
					charged:	$

a. ☒ A check in the amount of $ 972.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-0916. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING**: Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P
1300 I Street, N.W.
Washington, D.C. 20005-3315
EFC/FPD/sci
DATED: February 27, 2001

SIGNATURE
Ernest F. Chapman/25,961
NAME/REGISTRATION NO.

PATENT
Customer Number 22,852
Attorney Docket No. 2481.1726-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Petra LOOS et al.	)	Group Art Unit: Not yet assigned
	)	
U.S. National Filing of PCT/EP99/05980	)	Examiner: Not yet assigned
	)	
Serial No.: Unknown	)	
	)	
Filed: February 27, 2001	)	
	)	

For: MINI-BASKET FOR ANALYZING ACTIVE SUBSTANCE RELEASE FROM A MEDICAMENT FORM

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Prior to the examination of the above application, please amend this application as follows:

IN THE SPECIFICATION:

Please amend the specification as follows with reference to the page lines as numbered:

Page 1, line 7, change "consisting of" to –including--; and

line 8, change "said" to –the--.

Page 3, line 35, change "consisting of" to –including--.

Page 4, line 5, change "particularly" to –more--, insert –fixing-- before "devices"; and

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line 15, replace "which consists for example of stainless steel" to –which can be made, for example, of stainless steel, and--.

Page 5, line 8, insert the following paragraph: -- There are two drawings. Fig. 1 is an isometric view of an embodiment of a device according to the present invention; and Fig. 2 is an isometric view of another embodiment of a device according to the present invention.";

line 9, change "Figure" to --Fig.--;

line 16, change "consisting of" to –includes--;

line 31, change "said" to –the--; and

line 32, after "a" insert –handle, e.g.,--.

Page 6, line 12, after "mini-basket" insert --,shown in Fig. 2,--, and after "(lid)" insert --3a--;

line 13, after "mini-basket" insert --2--;

line 14, after "rod" insert --5a--; and

line 15, after "clips" insert --6--.

IN THE CLAIMS:

Please cancel claims 1-7 and add new claims 8-31:

8. A device configured to fit within an in vitro substance release testing apparatus, the device comprising:

a mesh basket configured to receive a material to be tested; and

a lid including a handle on one side of the lid.

9. The device of claim 8, wherein the lid includes at least one fixing clip on a side of the lid opposite the handle.

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10. The device of claim 8, wherein the basket is cylindrical in shape and includes an open end and a closed end.

11. The device of claim 10, wherein the basket includes a narrow metal band around at least an open end of the basket.

12. The device of claim 8, wherein the handle includes a bracket configured to allow removal of the device from the testing apparatus.

13. The device of claim 8, wherein the device is configured to fit within a paddle agitator.

14. The device of claim 8, wherein the device is configured to fit within a continuous flow cell.

15. The device of claim 8, wherein the device is configured to fit within a rotating basket apparatus.

16. The device of claim 8, wherein the device is configured to fit within a paddle agitator and a continuous flow cell.

17. The device of claim 8, wherein the material to be tested is a medicament in solid form.

18. The device of claim 8, wherein the lid is formed of a mesh material.

19. The device of claim 8, wherein the lid is a plate.

20. The device of claim 18, wherein the handle is attached to the lid in a manner which maximizes the amount of the lid surface through which a fluid may pass.

21. The device of claim 9, wherein the fixing clip is configured to connect the lid to the basket.

22. The device of claim 9, wherein the lid includes three fixing clips.

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23. The device of claim 19, wherein the handle includes a rod.

24. The device of claim 8, wherein the mesh forming the basket is a wire screen fabric.

25. A method of testing, in vitro, active substance release from a medicament in solid form, comprising:

providing a device configured to fit within an in vitro substance release testing apparatus comprising a mesh basket configured to receive a material to be tested and a lid including a handle on one side of the lid;

placing the solid medicament to be tested in the basket;

placing the device in a paddle agitator;

testing the medicament in an acid release medium of a given pH;

removing the device from the paddle agitator;

placing the device into a continuous flow cell; and

testing the medicament form at a higher pH.

26. The method of claim 25, wherein removing the device includes lifting the device out of the paddle agitator by the handle.

27. The method of claim 25, further including securing the lid to the basket via at least one fixing clip.

28. A method of testing, in vitro, active substance release from a coated solid medicament, comprising:

providing a device configured to fit within an in vitro substance release testing apparatus comprising a mesh basket configured to receive a material to be tested and a lid plate including a rod attached to one side of the lid plate;

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placing the coated solid medicament to be tested in the basket;

placing the device in a rotating basket apparatus;

testing the integrity of the coating of the medicament in an acid release medium of a given pH;

removing the device from the rotating basket apparatus;

removing the lid plate from the basket;

placing a mesh lid with a handle onto the basket;

placing the device into a continuous flow cell; and

testing the medicament at a higher pH.

29. The method of claim 28, wherein removing the device includes lifting the device out of the rotating basket apparatus by the rod attached to the lid plate.

30. The method of claim 28, further including securing the lid plate to the basket via at least one fixing clip.

31. The method of claim 28, further including securing the mesh lid to the basket via at least one fixing clip.

IN THE DRAWINGS:

Please add new Fig. 2. Fig. 2 has been added to illustrate the second embodiment of the lid of the device, as set forth in the specification on page 6, lines 12-20, and as claimed in claims 19, 23, and 28-31. No new matter has been added.

REMARKS

Claims 1-7 have been cancelled and new claims 8-31 have been added to place the application in proper form for U.S. examination. The specification has been

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amended to conform with U.S. practice. New Fig. 2 has been added to illustrate a second embodiment of the invention as claimed.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: February 27, 2001

By: Elizabeth M Burke
Elizabeth M. Burke
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PATENT
Customer Number 22,852
Attorney Docket No. 2481.1726-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Petra LOOS et al.

U.S. National Filing of PCT/EP99/05980

Serial No.: Unknown

Filed: February 27, 2001

For: MINI-BASKET FOR ANALYZING ACTIVE SUBSTANCE RELEASE FROM A MEDICAMENT FORM

Group Art Unit: Not yet assigned

Examiner: Not yet assigned

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

REQUEST FOR APPROVAL OF DRAWING CHANGE

Subject to the approval of the Examiner, it is respectfully requested that new Fig. 2 be added to the above-captioned application. A copy of new Fig. 2 is attached.

Upon approval of the proposed changes, applicants respectfully request that the submission of revised drawings be deferred until after a notice of allowance has issued.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: February 27, 2001

By: Elizabeth M. Burke
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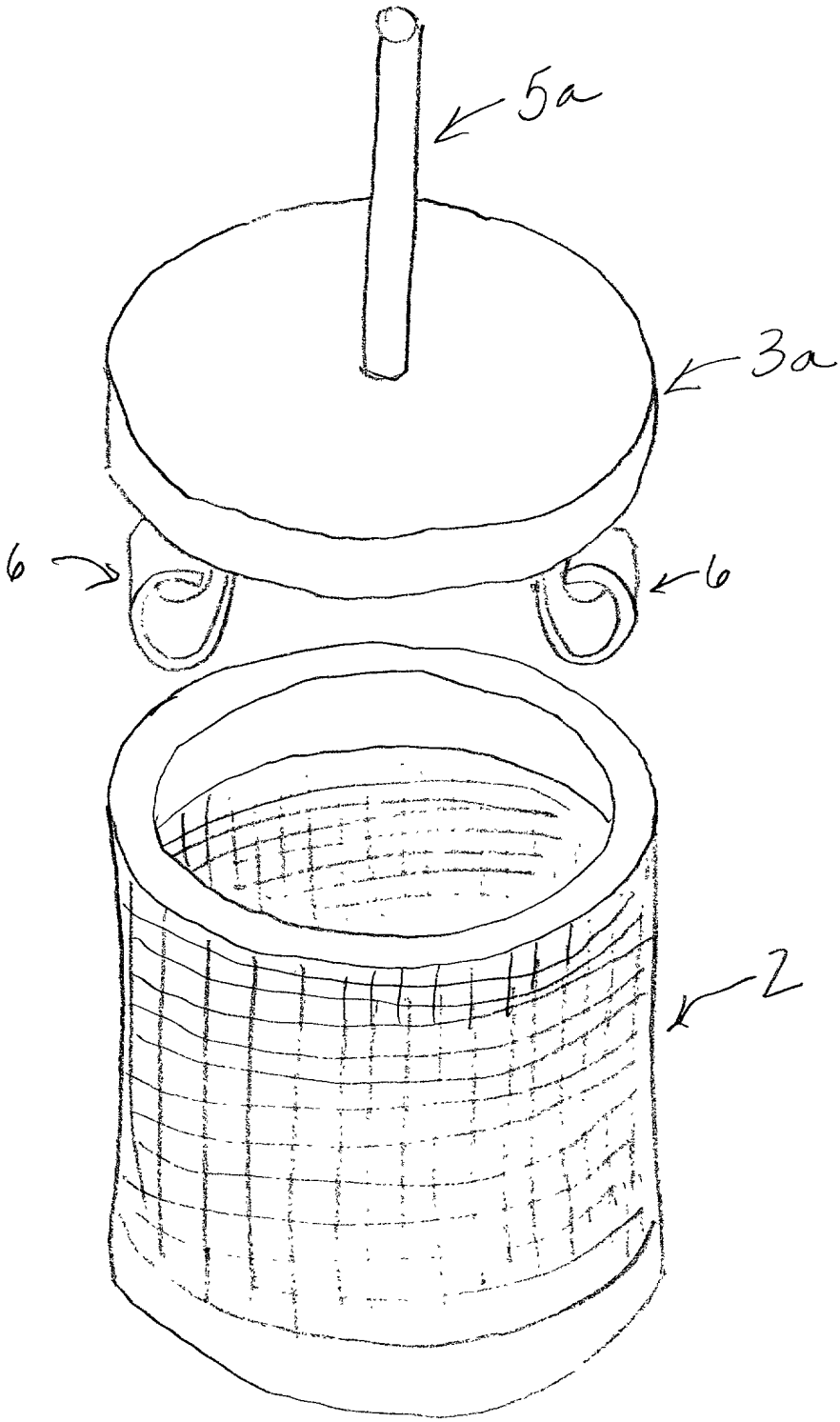

Fig. 2

Description

Mini-basket for analyzing active substance release from a medicament form

The following describes a device for analyzing in vitro active substance release from a solid medicament form, consisting of a novel mini-basket, and the use of said device.

During the development of a medicament form, the quality, efficacy and safety of the drug are tested inter alia by in vivo and in vitro analyses. The in vitro analyses are of particular importance as they are often able to demonstrate small changes in the medicament form which could affect its efficacy and tolerability (and thus the drug safety). By means of in vitro release analyses, the pharmaceutical formulation can be optimized while minimizing cost-intensive and time-consuming in vivo studies, and the quality of the manufactured batches can be monitored during development, storage and production (notes to DAB 1996, V.5.4. Active substance release from solid oral medicament forms, Govi-Verlag, published by Hartke, Hartke, Mutschler, Rücker, Wichtl). Comparing in vitro data results with in vivo studies can reduce the number of tests carried out on humans and animals, since conclusions can be drawn concerning the in vivo results in later samples.

An important condition for active substance absorption, and thus for bioavailability, is the active substance release from the medicament form (notes to DAB 1996, V.5.4. Active substance release from solid oral medicament forms, Govi-Verlag, published by Hartke, Hartke, Mutschler, Rücker, Wichtl). The pharmacopeias describe for this purpose a number of official in vitro release analysis methods with the known apparatuses associated with these methods. Thus, to determine the release of active substances from solid medicament forms such as tablets, capsules, pellets or suppositories, use is made of paddle agitators, rotating baskets and continuous flow cells. The first of these are closed systems in which the medicament form to be tested is located either in the cylindrical vessel belonging to the apparatus or in the rotating basket itself, and the paddle agitator and rotating basket serve for agitation. The continuous flow cell apparatus can be used as a closed system (return of the release medium) or as an open system (delivery of fresh release medium). Test liquid is

removed at set times and the medicament which has dissolved in it is measured. These apparatuses, paddle agitator apparatus, rotating basket apparatus and continuous flow cell, are known from European Pharmacopeia 1997, Govi-Verlag, pages 136 through 139, or from the US Pharmacopeia, The United States Pharmacopoeial Convention Inc., Twinbrook Parkway, Rockville, MD, pages 1791 through 1799 (USP 23/NF 18).

Medicament forms with modified active substance release include coated or uncoated medicament forms in which the rate of release or the site of release is deliberately changed. In addition, there are enteric-coated medicament forms which are resistant in the gastric juice and release the active substance in the intestinal juice. If the active substance is readily soluble in the release medium, these medicament forms can be tested with the aforementioned apparatuses (paddle agitator apparatus and rotating basket apparatus) after appropriate validation. In some cases the continuous flow cell is also used, especially if release profiles are to be recorded. The so-called sink conditions should be maintained during testing, i.e. the concentration of the active substance to be tested in the release medium should not exceed 30% of the saturation concentration.

In contrast to the observations made above, the analysis of in vitro active substance release from medicament forms with medicament substances which are sparingly soluble in the release medium can be problematic in the known paddle agitator and rotating basket apparatuses since, because of the limited volume, the release can be controlled by the solubility of the active substance and not by the delivery from the medicament form. In this case, the known continuous flow cell (as open system) can be of help since it continuously delivers fresh release medium. If the medicament form containing the sparingly soluble active substance is not enteric-coated, the use of the continuous flow cell is a suitable method for indicating the release profiles of medicament forms with modified active substance release. However, in the case of enteric-coated medicament forms, the integrity of the coating must be tested before the actual test of active substance release, i.e. the latter is preceded by an analysis step in an acid release medium. Should the analysis be carried out with the continuous flow cell, a pH gradient may develop in the first collected fractions, and this can falsify the results.

An enteric-coated medicament form can, for example, be a capsule containing the active substance enclosed in so-called pellets. These pellets can be enteric-coated, i.e. they are intended to release the active substance only at higher pH values, such as those obtained during passage through the intestinal tract. Consequently, these pellets become less and less stable as pH values increase, i.e. they release the active substance relatively rapidly in release media with higher pH values. In some circumstances it is no longer possible to differentiate between smaller formulation differences. If at the same time the active substance is only sparingly soluble in media with lower pH values, the result in this case does not point to the release from the medicament form, but instead is controlled by the solubility of the active substance. Although a release medium with a high pH value can obviate this, it cannot however be used on account of the aforementioned difficulty (poor differentiation).

A release medium with a moderate pH value, used in the known continuous flow cell apparatus, can on the one hand discriminate between different formulations and, on the other hand, can permit a release analysis by means of delivering fresh medium to avoid the solubility problems. A method is known from DE 29 42 129 A1 in which the dissolver chambers of at least two continuous flow cells are connected to each other. The aim of this is to ensure a controlled passage of dissolving medium with medicament particles or medicament forms from one cell to the next. In this particular case, however, it has been found to be difficult to analyze the resistance to gastric juice. On account of the pH gradient in the first basic fraction following previous use of an acid medium (acid residue liquid is necessarily still present in the hose system of the apparatus), the active substance precipitates and cannot be completely analyzed.

The object of the invention is therefore to develop a device for analyzing in vitro active substance release, with which device these disadvantages are eliminated.

The subject of the invention is a device for in vitro active substance release from a solid medicament form, consisting of a mini-basket, characterized in that the bottom part (mini-basket) and the top part (lid) of the mini-basket are made of wire screen fabric, and the top part (lid) has a handle on the outer side.

Analyses are carried out on solid medicament forms, for example tablets, capsules, pellets, suppositories, or preferably enteric-coated medicament forms. The inside of the lid is secured with frictional engagement on the upper side of the mini-basket by means of one or more, preferably one to three, fixing clips, particularly preferably one fixing clip, or other devices, among other reasons so that the mini-basket can be fitted flush into the known continuous flow cells (type A and type B) (see European Pharmacopeia 1997, Govi-Verlag, pages 136 – 139, and also other pharmacopeias). The fixing clip is arranged, e.g. welded, centrally on the inside of the lid for example, without reducing the size of the wire screen fabric. Other fixing clips made of metal are also possible, for example arranged on the edge of the lid, or fixing clips without central section. The mini-basket of welded wire screen fabric is shaped as a cylinder whose upper and lower edges are enclosed by a narrow metal band. The wire screen fabric, which consists for example of stainless steel, can also be coated with a suitable material (e.g. gold), depending on the test liquid, in order to ensure that these parts do not react with the formulation being tested or with the test liquid or influence the response. The wire screen fabric can run in any desired direction, i.e. vertically/horizontally or also diagonally, but preferably vertically/ horizontally.

The dimensions of the mini-basket can vary depending on the in vitro release analysis which has been chosen. The following are approximate values. The height can in general be freely chosen, and depending on the continuous flow cell the maximum height of the mini-basket is 35 or 50 mm. Thus, for example, baskets can be used having a height of L (total height) = 10 mm to 40 mm, preferably = 20 mm, L_1 (height of the wire screen fabric) preferably = 16 mm, L_2 (height of the top metal band) preferably = 1 mm, L_3 (height of the bottom metal band) preferably = 3 mm, and a diameter of D (total diameter of the base) = 11.5 mm to 22.6 mm, preferably 11.9 mm (continuous flow cell type B) and 22.5 mm (continuous flow cell type A), particularly preferably = 22.5 mm (i.e. flush with the diameter of the chosen continuous flow cell), D_1 (diameter of the wire screen fabric) preferably = 16.5 mm, D_2 (diameter/width of the metal band) preferably = 3 mm, and lid whose diameter corresponds to that of the mini-basket and whose height corresponds to the width of the metal band L_3 (height of the metal band) preferably = 3 mm. The size and the material of the handle can vary, but complies with that of the mini-basket. The design of the handle is such that the mini-basket can be easily removed from the

in vitro active substance release apparatus. A bracket, stirrup, knob, rod or eyelet can be used, for example, or a combination of rod and eyelet is conceivable, but a bracket is preferable. The attachment of the handle on the lid, centrally or at the lid edge (metal band), should be done as far as possible without reducing the size of the wire screen fabric surface. The handle can for example be welded, screwed or riveted onto the lid, the latter attachment forms can also include the fixing clip.

An illustrative embodiment of the invention is represented in Figure 1 and is explained in greater detail below:

The mini-basket (1), whose dimensions are preferably chosen (see last but one paragraph) such that it can be introduced flush into the appropriate apparatuses depending on the in vitro release analysis to be carried out (e.g. paddle agitator and/or continuous flow cells type A or type B), consists of a bottom part (mini-basket) (2) and of a top part (lid) (3) whose dimensions are determined by the chosen in vitro release method(s) and the associated size(s) of the apparatuses. The mini-basket (2) is made of welded wire screen fabric and is cylindrical in shape. The wire thickness of the wire screen fabric (d) can be from 0.1 to 0.3 mm for example, preferably from 0.2 to 0.3 mm and particularly preferably 0.254 mm. The clear mesh width can be chosen, depending on the medicament form to be analyzed, to be from 0.1 mm up to the diameter of the particle to be analyzed, preferably from 0.2 to 1 mm, particularly preferably 0.55 mm. The top edge and bottom edge of the mini-basket (2), the edge of the lid (3) and the edges of the base plate of the mini-basket and the upper face of the lid are enclosed by a narrow metal band (4), preferably of the same material as the wire screen fabric. The edge of the lid (3) ends flush with the upper edge of the mini-basket (2). In addition, lid (3) and mini-basket (2) are held together frictionally by a fixing clip (6) which inter alia can have the width of the metal band, without said fixing clip (6) reducing the size of the wire screen fabric. The lid (3) is provided with a bracket (5) of the same material. The bracket is used for lifting the mini-basket out of the in vitro active substance release apparatus. The dimensions of the bracket secured on the lid or also of the other handles can vary, preference being given to a height of 4 mm and a width of 2 mm in the case of the bracket.

The subject of the invention is also a method for in vitro active substance release from a solid medicament form (e.g. tablets, capsules, pellets),

preferably enteric-coated pellets, by testing in acid release medium and subsequently at a higher pH, which method is characterized in that a mini-basket as described above, containing the solid medicament form, is placed in a vessel of a known paddle agitator, the integrity of the coating is tested in the acid release medium, the mini-basket is then lifted out of the vessel of the known paddle agitator with the aid of the handle located on the lid, and it is introduced into a known continuous flow cell, and the release of the active substance from the medicament form is tested at a higher pH. The mini-basket is constructed such that it fits flush into the cell and the test medium can flow through the meshes.

A further embodiment of the mini-basket differs in that it has a top part (lid) modified to the dimensions of the mini-basket and in the form of a plate to which a rod is secured (e.g. welded) and which has one or more, preferably one to three, fixing clips which hold the mini-basket securely and permit a rotation concentric to the axis of the mini-basket, comparable with the rotating basket apparatus described in European Pharmacopeia 1997, Govi-Verlag, page 137. Except for the lid, the novel mini-basket corresponds to the description given above. An operation similar to the known rotating basket apparatus is therefore possible.

A subject of the invention is therefore a method for in vitro active substance release from a solid medicament form by testing in acid release medium and subsequently at a higher pH, characterized in that a mini-basket with rod, as described in the previous paragraph, containing the solid medicament form is placed in a vessel of a known rotating basket apparatus and the integrity of the coating is tested in the acid release medium, after which the mini-basket is lifted out of the vessel of the rotating basket apparatus, the lid in the form of a plate with rod is replaced by a corresponding wire screen fabric lid with handle, as described above, and introduced into a known continuous flow cell with the aid of the handle, and the release of the active substance from the medicament form is tested at a higher pH. The medicament form to be analyzed can therefore likewise be analyzed in the rotating basket apparatus and then in the continuous flow cell.

Using the mini-basket, it is therefore possible to exploit the advantages of different systems for testing the in vitro active substance release from complicated solid oral medicament forms. The active substance release

can be performed in one analysis operation, the results of which can improve drug safety.

Patent Claims:

1. A device for in vitro active substance release from a solid medicament form, consisting of a mini-basket with a bottom part and a top part, the bottom part (mini-basket) and the top part (lid) of the mini-basket being made of wire screen fabric, and the top part (lid) having a handle on the outer side.

2. The device as claimed in claim 1, characterized in that the bottom part (mini-basket) is connected to the top part (lid) by one or more fixing clips.

3. The device as claimed in claims 1 and 2, characterized in that the bottom part (mini-basket) is connected to the top part (lid) by one fixing clip.

4. The device as claimed in claims 1 through 3, characterized in that the removal device is a bracket.

5. Use of a device as claimed in claims 1 through 4 in a paddle agitator and/or continuous flow cell.

6. A method for in vitro active substance release from a solid medicament form by testing in acid release medium and subsequently at a higher pH, characterized in that a mini-basket as claimed in claims 1 through 4, containing the solid medicament form, is placed in a vessel of a known paddle agitator, the integrity of the coating is tested in the acid release medium, the mini-basket is then lifted out of the vessel of the known paddle agitator with the aid of the handle located on the lid, and it is introduced into a known continuous flow cell, and the release of the active substance from the medicament form is tested at a higher pH.

7. A method for in vitro active substance release from a solid medicament form by testing in acid release medium and subsequently at a higher pH, characterized in that a mini-basket containing the solid medicament form and consisting of a bottom part (mini-basket) of wire screen fabric and a top part (lid) in the form of a plate, to which a rod is attached and which has one or more fixing clips holding the mini-basket

and the lid together frictionally and permitting a rotation concentric to the axis of the mini-basket, is placed in a vessel of a known rotating basket apparatus and the integrity of the coating is tested in the acid release medium, after which the mini-basket is lifted out of the vessel of the rotating basket apparatus, the lid in the form of a plate is replaced by a corresponding wire screen fabric lid with handle and introduced into a known continuous flow cell, and the release of the active substance from the medicament form is tested at a higher pH.

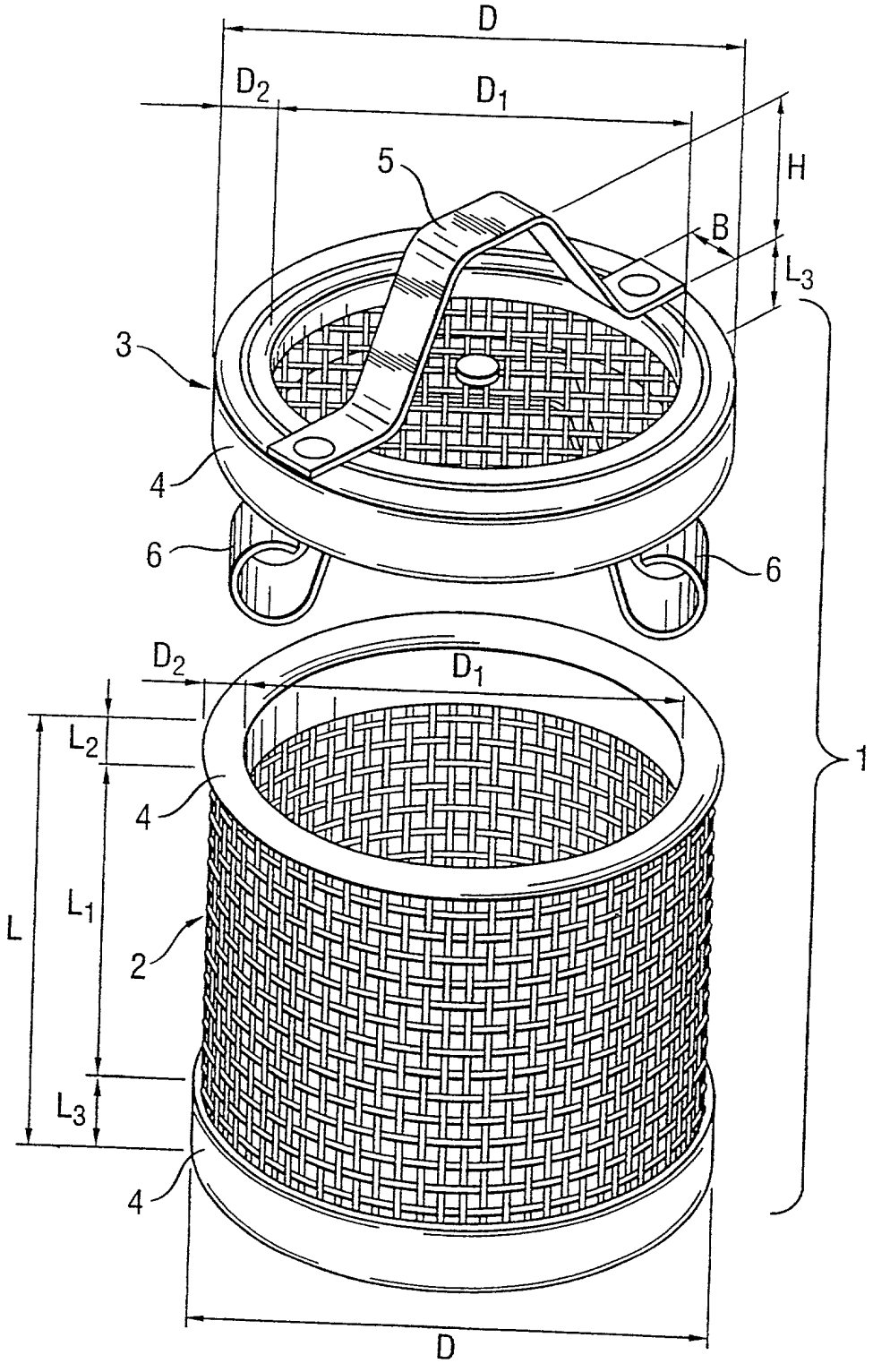

Fig. 1

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

As below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below, I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

Mini-basket for analyzing active substance release from a medicament form

the specification of which

was filed on August 14, 1999 as International Patent Application PCT/EP99/05980.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s) for which Priority is Claimed:

Federal Republic of Germany, 19839398.9-52 of August 29, 1998

And I hereby appoint
Douglas B. Henderson, Reg.No. 20,291; Arthur S. Garrett, Reg.No. 20,338
Jerry D. Voight, Reg.No. 23,020; Herbert H. Mintz, Reg.No. 26,691;
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all of the firm of FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, Reg.No. 22,540, my attorneys, with full power of substitution and revocation to prosecute this application, to make alterations and amendments therein, to file continuation and divisional applications thereof, to receive the Patent, and to transact all business in the Patent and Trademark Office and in the Courts in connection therein, and specify that communications about the application are to be directed to the following correspondence address:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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